(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 21 October 2004 (21.10.2004)

(51) International Patent Classification 7.

PCT

COIN TOUCO

(10) International Publication Number WO 2004/090551 A3

(51)	International Patent Ci	assincation': GUIN 33/68	Guilaine [FR/CH]; c/o GeneProt, Inc., 2, Pre-de-la-	
(21)	International Application	on Number: PCT/EP2004/003737	Fontaine, 1217 Meyrin (CH). BEDERR, Nassima [FR/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine.	
(22)	International Filing Dat		CH-1217 Meyrin (CH). BOUGUELERET, Lydie [FR/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine.	
(25)	Filing Language:	English	CH-1217 Meyrin (CH). CUSIN, Isabelle [FR/CH]:	
(26)	Publication Language:	English	c/o GeneProt, Inc., 2, rue Pre-de-la-Fontaine, CH-1217 Meyrin (CH). MAHE, Eve [FR/CH]; c/o GeneProt, Inc., 2,	
(30)	Priority Data:		Pre-de-la-Fontaine, CH-1217 Meyrin (CH). NIKNEJAD,	
	_	8 April 2003 (08.04.2003) US	Anne [CH/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine	
	60/461,623	8 April 2003 (08.04.2003) US	CH-1217 Meyrin (CH). REFFAS, Samia [CH/CH]; c/o	

US

US

(CH).

- 60/474,863 30 May 2003 (30.05.2003) US 60/484,140 30 June 2003 (30.06.2003) US (71) Applicant (for all designated States except US): GEN-OVA, LTD.; Canon's Court, 22 Victoria Street, Hamilton,
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60/471,479

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GeneProt, Inc., 2, Pre-de-la-Fontaine, CH-1217 Meyrin

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

[Continued on next page]

(54) Title: SECRETED POLYPEPTIDE SPECIES ASSOCIATED WITH CARDIOVASCULAR DISORDERS

SEQ ID NO:1

- APGPRGIIIN LENGELCMNS AQCKSNCCQH SSALGLARCT SMASENSECS VKTLYGIYYK 1
- CPCERGLTCE GDKTIVGSIT NTNFGICHDA GRSKQ 61

16 May 2003 (16.05.2003)

SEQ ID NO:2

- GIIINLENGE LCMNSAQCKS NCCQHSSALG LARCTSMASE NSECSVKTLY GIYYKCPCER 1
- 61 GLTCEGDKTI VGSITNTNFG ICHDAGRSKQ

SEQ ID NO:3

1 SNCCQHSSAL GLAR

SEQ ID NO:4

1 CTSMASENSE CSVK

SEQ ID NO:5

1 TIVGSITNTN FGICHDAGR

(57) Abstract: The invention discloses human secreted polypeptides that circulate at an increased level in the plasma of patients with cardiovascular disorders. The invention also provides methods of using compositions including the polypeptides, polynucleotides encoding them, and antibodies specific for these polypeptides, for diagnosis, prognosis, and for drug development.



PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 20 January 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

International Application No

T/EP2004/003737

A 01 4 66	NEIO A TION OF OUR PROPERTY.		1-01/21/2004/003/3/		
ÎPC 7	SIFICATION OF SUBJECT MATTER G01N33/68				
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	data base consulted during the international search (name of	data base and, where practical,	search terms used)		
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C. DOCUM	IENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of	f the relevant passages	Relevant to daim No.		
A	CHAPUS C ET AL: "ROLE OF COL INTERFACIAL ADSORPTION OF PAN LIPASEAT HYDROPHILIC INTERFAC	1-16			
	FEBS LETTERS, ELSEVIER SCIENCE AMSTERDAM, NL, vol. 58, no. 1,				
	1 October 1975 (1975-10-01), 155-158, XP002041838 ISSN: 0014-5793 the whole document				
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	ner documents are listed in the continuation of box C.	X Patent family me	embers are listed in annex.		
"A" docume	legories of cited documents : Int defining the general state of the art which is not be of particular relevance	or phonity date and i	shed after the International filing date not in conflict with the application but the principle or theory underlying the		
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later th	document published prior to the international filing date but in the art. later than the priority date claimed "&" document member of the same patent family				
Date of the a	ctual completion of the international search	Date of mailing of the	International search report		
16	5 August 2004	2 5	3. 11. 2004		
vame and m	alling address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL ~ 2280 HV Rijswijk	Authorized officer			
	Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Weijland	Weijland, A		

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PCT/EP2004/003737

C/Cardiana No. 2001/15/17 2004/003737				
ation) DOCUMENTS CONSIDERED TO BE RELEVANT				
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
MAHE-GOUHIER N ET AL: "IMMOBILIZED COLIPASE AFFINITIES FOR LIPASES B, A, C AND THEIR TERMINAL PEPTIDE (336-449): THE LIPASE RECOGNITION SITE LYSINE RESIDUES ARE LOCATED IN THE C-TERMINAL REGION" BBA - LIPIDS AND LIPID METABOLISM, ELSEVIER SCIENCE BV. AMSTERDAM, NL, vol. 962, 1988, pages 91-97, XP002041839 ISSN: 0005-2760 the whole document	1-16			
WO 03/023397 A (LIU KAN-ZHI; MANTSCH HENRY H (CA); NAT RES COUNCIL (CA); SHAW ANTHONY) 20 March 2003 (2003-03-20) the whole document	1–16			
US 6 503 540 B1 (BADER DAVID M ET AL) 7 January 2003 (2003-01-07) the whole document	1–16			
WO 98/30588 A (CHAPUS CATHERINE ; LAPHAL LABORATOIRE DE PHARMACO (FR)) 16 July 1998 (1998-07-16) abstract page 3, paragraph 6	8,13			
WO 02/06840 A (BIOPREVENTIVE LTD; GALILI NACHSHON NITSA (IL); RUBIN YORAM (IL); NIMR) 24 January 2002 (2002-01-24) the whole document	1-16			
WO 98/17807 A (BIOCEM S A; MEROT BERTRAND (FR); BOURNAT PHILIPPE (FR); GRUBER VERONI) 30 April 1998 (1998-04-30) page 25, line 1 - line 17	9,10			
	COLIPASE AFFINITIES FOR LIPASES B, A, C AND THEIR TERMINAL PEPTIDE (336-449): THE LIPASE RECOGNITION SITE LYSINE RESIDUES ARE LOCATED IN THE C-TERMINAL REGION" BBA - LIPIDS AND LIPID METABOLISM, ELSEVIER SCIENCE BV. AMSTERDAM, NL, vol. 962, 1988, pages 91-97, XP002041839 ISSN: 0005-2760 the whole document WO 03/023397 A (LIU KAN-ZHI; MANTSCH HENRY H (CA); NAT RES COUNCIL (CA); SHAW ANTHONY) 20 March 2003 (2003-03-20) the whole document US 6 503 540 B1 (BADER DAVID M ET AL) 7 January 2003 (2003-01-07) the whole document WO 98/30588 A (CHAPUS CATHERINE; LAPHAL LABORATOIRE DE PHARMACO (FR)) 16 July 1998 (1998-07-16) abstract page 3, paragraph 6 WO 02/06840 A (BIOPREVENTIVE LTD; GALILI NACHSHON NITSA (IL); RUBIN YORAM (IL); NIMR) 24 January 2002 (2002-01-24) the whole document WO 98/17807 A (BIOCEM S A; MEROT BERTRAND (FR); BOURNAT PHILIPPE (FR); GRUBER VERONI) 30 April 1998 (1998-04-30)			

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

Information on patent family members

International Application No

	Patent document ed in search report		Publication date		Patent family member(s)	Publication date
WO	03023397	Α	20-03-2003	CA	2357338 A1	12-03-2003
			,	WO	03023397 A1	20-03-2003
				CA	2459349 A1	20-03-2003
				EP	1428022 A1	16-06-2004
US 	6503540	B1	07-01-2003	NONE	,	
WO	9830588	Α	16-07-1998	FR	2758143 A1	10-07-1998
				ΑT	273995 T	15-09-2004
				AU	727469 B2	14-12-2000
				AU	5868698 A	03-08-1998
				BR	9806857 A	14-03-2000
				CA	2277778 A1	16-07-1998
				CN	1248264 T	22-03-2000
				CZ	9902414 A3	12-01-2000
				DE	69825733 D1	23-09-2004
				EP	0970118 A1	12-01-2000
				WO	9830588 A1	16-07-1998
				HU	0001458 A2	28-10-2000
				NZ	337087 A	26-01-2001
				US	6432400 B1	13-08-2002
				ZA	9800094 A	08-07-1998
WO	0206840	Α	24-01-2002	AU	7272801 A	30-01-2002
				CA	2414897 A1	24-01-2002
				EP	1299731 A2	09-04-2003
				WO	0206840 A2	24-01-2002
				US 	2004015101 A1	22-01-2004
WO	9817807	Α	30-04-1998	FR	2754827 A1	24-04-1998
				AU	4871997 A	15-05-1998
				CA	2269025 A1	30-04-1998
				EP	0941343 A1	15-09-1999
				MO	9817807 A1	30-04-1998
				JP	2001507928 T	19-06-2001

International application No. PCT/EP2004/003737

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 14-16 (with respect to industrial applicability) because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 14-16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
A. X No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-16 (part)
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

- 1. claims: 1-16 (partially)
 - 1. Claims 1-16 (partially)
 Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of a treatment etc. using SEQ ID NOs 1-5 involving colipase
- 2. claims: 1-16 (partially)
 - 2. Claims 1-16 (partially)
 Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc. using SEQ ID NOs 6-10 involving eosinophil-derived neurotoxin
- 3. claims: 1-16 (partially)

Claims 1-16 (partially)
Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc using SEQ ID Nos 11-14 involving human epididymal secretory protein.

4. claims: 1-16 (partially)

Claims 1-16 (partially)
Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc. using SEQ ID NOS 15-23 involving Defensin I

5. claims: 1-16 (partially)

Claims 1-16 (partially)
Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc. using SEQ ID NOs 24-28 involving plasminogen-related protein B

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